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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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			1642	

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Please find below and/or attached an Office communication concerning this application or proceeding.

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Office Action Summary	Application No.	Applicant(s)	
	10/736,112	ROSS, JEFFREY S.	
	Examiner	Art Unit	
	MINH-TAM DAVIS	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 17 October 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-40 is/are pending in the application.
- 4a) Of the above claim(s) 17-32 and 35-40 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-16, 33 and 34 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>09/20/04; 01/13/06</u> | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Applicant's election with traverse of group I, claims 1-16, 33-34 in the reply filed on 10/17/06 is acknowledged.

The traversal is on the ground(s) that it would not be unduly burden for the Examiner to examine both groups I and III, because the search of both of these groups require determining recurrence, by evaluating PSMA protein levels.

This is not found persuasive because it would be unduly burden for the Examiner to search both groups I and III. The searches for groups I and II are not extensive. The search of group III requires additional search for a method of treating prostate cancer, using a novel method, i.e. using an antibody to PMSA.

The requirement is still deemed proper and is therefore made FINAL.

Accordingly, group I, claims 1-16, 33-34, a method for determining if a subject is at risk for prostate cancer recurrence, comprising determining the protein PMSA level.

Specification

The amendment of the specification, submitted on 06/30/04, of the paragraph beginning on page 25, line 25, bridging page 26 to add sequence identification numbers is acknowledged and entered.

Objection

1. Claims 1-16, 33-34 are objected to, for the use of the abbreviation language 'PMSA' in claims 1, 3, 4, 15, 16. Amendment of the claims to replace "PMSA" with "prostate specific membrane antigen" is suggested.
2. Claims 1-16, 33-34 are objected to, for the use of the language "to" thereby determine in claim 1. This objection could be obviated by, for example, deleting the language "to".

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-16, 33-34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1. Claims 1-16, 33-34 are indefinite, because it is not clear which reference standard, as cited in claims 1, 3 is referred to, for use in the claimed method.

The specification discloses that the term "reference standard" as used here "can" refer to a standard that is statistically significant level of PSMA expression which distinguishes subjects having recurrence and subjects that do not have a recurrence (p.23, second paragraph).

In view of the non-limiting definition of 'reference standard', one cannot determine which standard is used as a reference standard for the claimed method.

2. Claim 4 is indefinite, because it is not clear how the control subject is distinguished from the tested subject, because both were diagnosed with prostate cancer.

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This rejection could be obviated, by amending the claim, for example, to add “a control subject previously diagnosed with prostate cancer before prostatectomy, but that does not have prostate cancer recurrence”.

3. Claims 33-34 are objected to, because the term a “higher” level of expression is a relative term. The term is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Claim Rejections - 35 USC § 112, First Paragraph, Written Description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-16, 33-34 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification discloses that PMSA is a transmembrane folate hydrolase consisting of 750 amino acids and having a molecular weight of 110 kDa (p.1, first two lines of the last paragraph).

In view of the non-limiting definition of PMSA, PMSA without being accompanied by a sequence identification number reasonably reads on a genus of variant transmembrane folate hydrolases.

Although drawn to DNA arts, the findings in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997) and Enzo Biochem, Inc. V. Gen-Probe Inc. are relevant to the instant claims. The Federal Circuit addressed the application of the written description requirement to DNA-related inventions in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). The court stated that “[a] written description of an invention involving a chemical genus, like a description of a chemical species, requires a precise definition, such as by structure, formula, [or] chemical name, of the claimed subject matter sufficient to distinguish it from other materials.” *Id.* At 1567, 43 USPQ2d at 1405. The court also stated that

a generic statement such as “vertebrate insulin cDNA” or “mammalian insulin cDNA” without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. *Id.* At 1568, 43 USPQ2d at 1406. The court concluded that “naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material.” *Id.*

Finally, the court addressed the manner by which a genus of cDNAs might be described. “A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the

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genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus.” Id.

The Federal Circuit has recently clarified that a DNA molecule can be adequately described without disclosing its complete structure. See Enzo Biochem, Inc. V. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). The Enzo court adopted the standard that □the written description requirement can be met by “show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristicsi.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics.” Id. At 1324, 63 USPQ2d at 1613 (emphasis omitted, bracketed material in original).

The inventions at issue in Lilly and Enzo were DNA constructs per se, the holdings of those cases are also applicable to claims such as those at issue here. A disclosure that does not adequately describe a product itself logically cannot adequately describe a method of using that product.

In this case, the specification does not describe PMSA protein in a manner that satisfies either the standards as shown in the example of Lilly or Enzo. The specification does not provide sufficient structure or common structure to support the broad breath of the claimed genus. Nor is there any functional characteristics coupled with a known or disclosed correlation between structure and function. Thus, the specification does not provide a description of PMSA protein, that would satisfy the standard as shown in the example of Enzo.

The specification also fails to describe PMSA protein, by the standards shown in the example in Lilly. The specification fails to describe a “representative number” of such species. In addition, the specification also does not describe “structural features common to the members of the genus, which features constitute a substantial portion of the genus.”

The specification does not provide an adequate written description of PMSA protein that is required to practice the claimed invention. Thus, the specification does not meet the 112, first paragraph written description requirement, and one of skill in the art would reasonably conclude that Applicant did not have possession of the claimed PMSA protein at the time the invention was made. Since the specification fails to adequately describe the product for use in the claimed method, it also fails to adequately describe the claimed method.

Claim Rejections - 35 USC § 112, First Paragraph, Enablement

Claims 1-16, 33-34 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

1. Claims 1-16, 33-34 and the specification are rejected under 35 U.S.C. 112, first paragraph, for incorporating the essential material, PSMA, by only a reference to publications. It is noted that PSMA is an essential material for the claimed method. However, the specification only defines PSMA by citing references known in the art (the instant specification, page 1, last paragraph, bridging page 2). MPEP 608.01 teaches that incorporation of **essential material** in the specification by reference to a foreign application or patent, or to a publication is improper.

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Applicant is required to amend the disclosure to include the material incorporated by reference (see 37 CFR 1.57). The amendment must be accompanied by an affidavit or declaration executed by the applicant, or a practitioner representing the applicant, stating that the amendatory material consists of the same material incorporated by reference in the referencing application. In re Hawkins, 486 F.2d 569, 179 USPQ 157 (CCPA 1973); In re Hawkins, 486 F.2d 579, 179 USPQ 163 (CCPA 1973); In re Hawkins, 486 F.2d 577, 179 USPQ 167 (CCPA 1973) (see MPEP 6.19 and 6.19.01). In other words, Applicant is required to submit a paper copy and a computer readable form copy of the PSMA sequence cited in the published reference as referred to in the specification, and a statement that the content of the paper and computer readable copies are the same, and include no new matter, as required by 37 CFR 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d). Applicant is also required to submit an affidavit or declaration executed by the applicant, or a practitioner representing the applicant, stating that the amendatory material consists of the same material incorporated by reference in the referencing application.

2. Further, Claims 1-16, 33-34 and the specification are also rejected under 35 U.S.C. 112, first paragraph, for lack of enablement for a method for determining if a subject is at risk for prostate cancer recurrence.

The following *Wands* factors have been considered when the 112, first paragraph, scope of enablement rejection was made.

The breadth of the claims

The breadth of the claims is broad.

The claims encompass a method for determining **risk** of prostate cancer recurrence, by determining an increased in protein level of **variant** PSMA proteins, as compared to a reference standard, or PSMA expression levels in a control subject diagnosed with prostate cancer.

The nature of the invention

The nature of the invention is complex. The claims encompass a method for determining risk of prostate cancer recurrence, by determining an increased in protein level of variant PSMA proteins.

The state of the prior art

The teaching in the art is controversial.

Bostwick et al, 1998 (Cancer, 82(11): 2256-2261) teach that the number of cells from 184 radical prostatectomies, that are immunoreactive to prostate specific membrane antigen (PSM), is **not predictive of recurrence** in the cohort of organ-confined, margin negative prostate cancers treated by surgery. Beckett et al, 1999 (Clin Cancer Res, 5 (12): 4034-40) teach that using Western blot, **serum** PSMA is not a prostate specific biomarker (see item under “The level of predictability in the art” below).

However, Rosenthal S A et al, 2001 (Techniques in Urology, 7(1): 27-37) teach that using an antibody to PSMA labeled with In 111 (or capromab pendetide), the positive predictive value (PPV) is 50% for prostatic fossa recurrence, and 62% for lymph node metastasis. Murphy et al, 1998 (Urology, 51: 89-97) teach that the PSMA value well above the normal range from 1

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to 4 years postoperatively corresponds best with a poor prognosis or suspected post-operative recurrence (see 102 rejection below).

None of the cited references however teach **confirmation** of the marker predictive value **in prospective population trials**, which is critical in view of the controversial data in the art.

The level of one of skill in the art

Although the level of skill in the field of molecular pathology is high, it would be undue experimentation for one of skill in the art to practice the claimed invention.

The level of predictability of the art

The level of unpredictability is high.

One cannot predict that the PMSA protein level could be successfully used as a predictor of recurrence of prostate cancer, in view of **contradictory** and conflicting teaching in the art, concerning utility of PSMA protein as a predictive marker for prostate cancer recurrence after prostatectomy, and further in view of a **lack of confirmation** of the marker predictive value **in prospective population trials** in the instant specification.

The following teaching in the art is contradictory to the claimed invention. Bostwick et al, 1998 (Cancer, 82(11): 2256-2261) teach that the number of cells from 184 radical prostatectomies, that are immunoreactive to prostate specific membrane antigen (PSM), is **not predictive of recurrence** in the cohort of organ-confined, margin negative prostate cancers treated by surgery (abstract, p.2259, second column, item under "Relationship between immunohistochemical expression and tumor recurrence", p.2260, first column, paragraph before

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last). Bostwick et al teach that prostate adenocarcinoma or high grade carcinoma has the most intense and extensive staining, and that local recurrence is observed in 23 patients (12.5%), systemic progression in 10 patients (5.4%) and PSA biochemical failure, i.e. PSA > 0.2 ng/ml at least 30 days after surgery, in 39 patients (21.2%) (p.2258, second column, p.2259, second column, item under). Similarly, Beckett et al, 1999 (Clin Cancer Res, 5 (12): 4034-40) teach that using Western blot, **serum** PSMA is not a prostate specific biomarker, and cannot be confirmed as having prognostic significance, because a variety of normal tissue such as small intestine and advancing age may contribute to the serum level of PSMA (abstract, p.4038, first column, last paragraph, and second column). This is confirmed by Thomas et al, 2002 (J Clin Oncology, 20(15): 3213-8), which teaches that the presence of circulating prostate cancer cells in the peripheral blood that express PSMA, as detected by PCR, is not a good indicator of the likelihood of recurrent or metastatic disease within 5 years of surgery (p. 3217, second column, last paragraph).

Further, the instant application only uses univariate analysis for correlating PSMA protein level with prostate cancer recurrence (p.34, first paragraph), without validating the data in a prospective population. However, the need to perform validation studies when characterizing putative biomarkers is clear in view of the teaching of Oesterreich, S et al, 1996 (Clin Cancer Res, 2: 1199-1206, especially p. 1205, first column, last three lines of paragraph before last). Oesterreich et al teach that **false positive correlation** can be obtained when **using the univariate analysis** to obtain a correlation of a marker with its prognostic value. Further, Tockman et al (Cancer Res., 1992, 52:2711s-2718s) teach considerations necessary in bringing a cancer biomarker (intermediate end point marker) to successful clinical application. Although

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the reference is drawn to biomarkers for early lung cancer detection, the basic principles taught are clearly applicable to the claimed invention. Tockman et al teaches that prior to the successful application of newly described markers, research must validate the markers against acknowledged disease end points, establish quantitative criteria for marker presence/absence and **confirm marker predictive value in prospective population trials** (emphasis added) (see abstract). Early stage markers of carcinogenesis have clear biological plausibility as markers of preclinical cancer and if validated can be used for population screening (p. 2713s, col 1). The reference further teaches that once selected, the sensitivity and specificity of the biomarker must be validated to a known (histology/cytology-confirmed) cancer outcome. The essential element of the validation of an early detection marker is the ability to test the marker on clinical material obtained from subjects monitored in advance of clinical cancer and link those marker results with subsequent histological confirmation of disease. This irrefutable link between antecedent marker and subsequent acknowledged disease is the essence of a valid intermediate end point marker (p. 2714, see Biomarker Validation against Acknowledged Disease End Points). Clearly, prior to the successful application of newly described markers, markers must be validated against acknowledged disease end points and the marker predictive value must be confirmed in prospective population trials (p. 2716s, col 2). Similarly, confirmation of prognosis ability of a marker protein is essential, in view of the teaching of Vandesompele J et al, 2003 (Oncogene, 22(3): 456-60). Vandesompele et al teach that the reported prognosis power of Id-2 expression in neuroblastoma cannot be confirmed, wherein Id-2 is assumed to be a direct target for MYCN protooncogene, the amplification of which is correlated with highly aggressive neuroblastoma. Thus without validation of the claimed method in a population of prostate cancer patients

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receiving prostatectomy, one cannot predict that overexpression of the PSMA protein level would be predictive of increased risk of prostate recurrence.

Further, one cannot predict that the protein level of the variant PSMA could be useful for predicting an increased risk of prostate cancer recurrence, because the protein expression level of **variant** PSMA proteins cannot be predicted, based on the expression level of the wild type PSMA protein. It is well known in the art that variants of a sequence do not necessarily express at the same level as the corresponding wild type. For example, Schmid S et al, 2001 (J comparative Neurology, 430(2): 160-71), teach that the variants flip/flop of the gene GluR are expressed at higher levels in neurons in the auditory brainstem, as compared to the wild type GluR-A and GluR-B, and that neurons in the central nucleus of the inferior colliculus express high levels of GluR-B flip but only low levels of the other receptor subunits. Conner et al, 1996 (Mol Brain Res, 42: 1-17), teach that full length trkB is found in the hippocampus in patients with Alzheimer's disease, but not in hippocampi of either normal age-matched individual or patients with Huntington's disease, and that truncated trkB is found in senile plaques in hippocampus and temporal lobe in both patients with Alzheimer's disease and Huntington's disease, but not in normal brains of age-matched individuals (page 8, item 3.1.2). Thus in view of the teaching in the art one cannot predict that the variant PSMA proteins would overexpress in prostate cancer tissue as compared to that of a reference standard, or of control subject diagnosed with prostate cancer, and therefore, one would not know how to use the claimed genus of variant PSMA proteins.

Working example, and the amount of direction provided by the inventor

The specification discloses that 57% of prostate cancer patients treated with prostatectomy and having overexpression of PSMA protein have recurrence of the disease by follow-up at 34 days after prostatectomy, as compared to 28% of prostate cancer patients treated with prostatectomy and having lower level of PSMA protein (table 1 on page 33, bridging page 34). The specification discloses that on multivariate analysis, advanced tumor stage and PSMA overexpression were independent predictors of biochemical recurrence (page 34, item under multivariate analysis for disease recurrence). The specification discloses that the PSMA protein over-expression is detected from prostate tissue of patients having organ confined cancer (61%), and advanced stages(39%) (p.33). The specification discloses that PSMA protein over-expression is defined by the presence of focal or diffuse intense staining in immunohistochemistry (p.33). The specification discloses that using Western blot, all prostate clinical tissues have some degree of immunodetectable PSMA protein, but increased levels are clearly evident in a subset of prostate cancers and the PIN specimen (p.34, under Western blotting).

The data disclosed in the instant specification, however, only indicates that overexpression of the PSMA protein level is **indicative** of recurrent prostate cancer. The specification lacks confirmation of the marker predictive value in prospective population trials.

It is noted that MPEP 2164.03 teaches that “the amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability of the art. In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The amount of guidance or direction refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in

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the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification.

In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as how to make and use the invention in order to be enabling."

Given the above unpredictability, and in view of the complex nature of the invention, a lack of sufficient disclosure in the specification, and the teaching in the art, which is contradictory to the claimed invention, it would have been undue experimentation for one of skill in the art to practice the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

1. Claims 1-3, 7-9, 11-16 are rejected under 35 U.S.C. 102(b) as being anticipated by
 - Rosenthal S A et al, 2001 (Techniques in Urology, 7(1): 27-37).

Claim 1 is drawn to: A method of determining if a subject is at risk for prostate cancer recurrence, the method comprising:

providing a sample from a subject; and

determining PSMA expression levels in the sample,

wherein increased PSMA expression levels relative to a reference standard are indicative of a risk of prostate cancer recurrence, to thereby determine if the subject is at risk of prostate cancer recurrence.

Claim 2 is drawn to: The method of claim 1, wherein the subject is diagnosed with prostate cancer.

Claim 3 is drawn to: The method of claim 1, wherein the increased PSMA levels are increased relative to a reference standard.

Claim 7 is drawn to: The method of claim 1, wherein the sample is a tissue sample from the subject.

Claim 8 is drawn to: The method of claim 7, wherein the tissue sample is a biopsy sample.

Claim 9 is drawn to: The method of claim 7, wherein the tissue sample is a sample from a prostatic or cancerous lesion.

Claims 11-13 are drawn to: The method of claim 1, wherein the risk of recurrence is determined upon diagnosis of prostate cancer (claim 11) or after the subject is diagnosed with prostate cancer (claim 12), or after the subject has been treated with an anti-cancer treatment (claim 13).

Claim 14 is drawn to: The method of claim 13, wherein the anti-cancer treatment is a radical or partial prostatectomy.

Claims 15-16 are drawn to: The method of claim 1, wherein PSMA expression levels are determined by determining the PSMA protein levels in a sample (claim 15), wherein PSMA protein levels are determined by a method selected from the group consisting of an enzyme-

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linked immunosorbent assay (ELISA), a radioimmunoassay (R/A), a Western blot, or an immunohistochemical assay (IHC) (claim 16).

Rosenthal et al teach that using an antibody to PSMA labeled with In 111 (or capromab pendetide), the positive predictive value (PPV) is 50% for prostatic fossa recurrence, and 62% for lymph node metastasis (abstract, tables 1-2 on pages 28-29). Rosenthal et al teach the normal biodistribution of the labeled antibody imaging is in figure 1, and increased uptake of the labeled antibody in the prostatic fossa after prostatectomy is in figure 2, wherein local recurrence is confirmed by biopsy (p.29, second column, last paragraph). Rosenthal et al teach that capromab pendetide imaging for evidence of metastasis provides prognostic information regarding which patients are most likely to benefit from postprostatectomy radiation therapy (p.34, second column, second paragraph). Rosenthal et al teach that prior to radical prostatectomy, capromab pendetide imaging should be optimally used in patients with negative bone scans (p.35, second column, second paragraph). Rosenthal et al teach that for patient with recurrent disease following primary therapy, the predictive value of capromab pendetide imaging of prostate or prostate fossa, however, is limited, due to lack of sensitivity of prostatic fossa biopsies; but providing valuable information when utilized along with other clinical, laboratory and available pathological information (p.34, first column).

It is noted that imaging of the radiolabeled antibody specific for PSMA reasonably reads on a radioimmunoassay, i.e. immunoassay of a radioactively labeled substance, wherein immunoassay is analysis and identification of a substance based on its antigenic actions.

All the limitations are met.

2. Claims 1-3, 5-6, 11-16 are rejected under 35 U.S.C. 102(b) as being anticipated by Murphy et al, 1998 (Urology, 51: 89-97).

Claim 1 is drawn to: A method of determining if a subject is at risk for prostate cancer recurrence, the method comprising:

providing a sample from a subject; and

determining PSMA expression levels in the sample,

wherein increased PSMA expression levels relative to a reference standard are indicative of a risk of prostate cancer recurrence, to thereby determine if the subject is at risk of prostate cancer recurrence.

Claim 2 is drawn to: The method of claim 1, wherein the subject is diagnosed with prostate cancer.

Claim 3 is drawn to: The method of claim 1, wherein the increased PSMA levels are increased relative to a reference standard.

Claims 5-6 are drawn to: The method of claim 1, wherein the sample is a fluid sample from the subject (claim 5), wherein the fluid is selected from the group consisting of serum, semen, and urine (claim 6).

Claims 11-13 are drawn to: The method of claim 1, wherein the risk of recurrence is determined upon diagnosis of prostate cancer (claim 11) or after the subject is diagnosed with prostate cancer (claim 12), or after the subject has been treated with an anti-cancer treatment (claim 13).

Claim 14 is drawn to: The method of claim 13, wherein the anti-cancer treatment is a radical or partial prostatectomy.

Claims 15-16 are drawn to: The method of claim 1, wherein PSMA expression levels are determined by determining the PSMA protein levels in a sample (claim 15), wherein PSMA protein levels are determined by a method selected from the group consisting of an enzyme-linked immunosorbent assay (ELISA), a radioimmunoassay (R/A), a Western blot, or an immunohistochemical assay (IHC) (claim 16).

Murphy et al teach that the PSMA value well above the normal range from 1 to 4 years postoperatively corresponds best with a poor prognosis or suspected post-operative recurrence (p.92, first column, last four lines bridging second column). Murphy et al teach that that the PSMA in serum sample is detected using Western blot, and that all patients samples are assessed against a healthy normal donor sample, and a prostate cancer patient sample with a high PSMA from the same Western blot as standards control (p.90, first column, item under PSMA assay). Murphy et al teach that the serum is from a population of patients from a screening group, a difficult diagnostic group, a pre- and postoperative radical prostatectomy, and from a group with metastatic disease, which population is followed for a serial period (abstract, item under "Methods", p.91, second column, first paragraph).

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MINH-TAM DAVIS whose telephone number is 571-272-0830. The examiner can normally be reached on 9:00 AM-5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, JEFFREY SIEW can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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MINH TAM DAVIS
November 06, 2006-


JEFFREY SIEW
SUPERVISORY PATENT EXAMINER